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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Paper No. 3012009

Application Number: 10/026,198
Filing Date: December 21, 2001
Appellant(s): Beil, Merrill

John F. Klos
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed December 1, 2008.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The following are the related appeals, interferences, and judicial proceedings known to the examiner which may be related to, directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal:

09//792,578

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The amendment after final rejection filed on February 4, 2005 has not been entered.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Listing of Evidence Relied Upon

The following is a listing of the prior art of evidence (e.g. patents, publications Official Notice, and admitted prior art) relied upon in the rejection of claims under appeal.

Number (Title)	Name	Date
5,240,675	Wilk et al	August 31, 1993
5,260,020	Wilk et al	November 9, 1993
5,262,401	Vogel et al	November 16, 1993
Inactivation of Gram-Negative Bacteria by Photosensitized Porphyrins	Nitzan et al	1992

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claims 1-3, 5-7, 9, 11, 15, 16, 19, 20, 22-25, and 30-32 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Vogel et al.

See column 11, line 8 to column 16, line 25.

Claims 1-4, 5-7, 9, 11, 15, 16, 18-20, 22-25, 30-34 and 40-52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wilk et al ('020) in combination with Wilk et al ('675)

and Vogel et al. Wilk et al ('020) teach sterilizing medical equipment such as catheters using light applied internally or externally of the surface. Wilk ('675) teach the use of the irradiation and a sterilizing solution. Vogel teach a solution as claimed that can be used in conjunction with light to kill bacteria or to treat viral conditions. It would have been obvious to the artisan of ordinary skill to employ in the method ofWilk et al ('675), the solution of Vogel et al to sterilize the long dwelling catheters etc of Wilk et al ('020), upon which biofilms form and to employ the method ofWilk et al ('675) on other body inserted lumens such as endotracheal tubes intravenous catheters, since these are equivalent to the catheters ofWilk et al ('020) and since these are also recognized in the art as sites which require sterilization, thus producing a method such as claimed.

Claims l, 5, 10-15, 20, and 26-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vogel et al in combination with Nitzan et al. Vogel et al teach a method of eradicating acellular or cellular organisms as claimed but does not teach adding the surface acting agent prior to the photosensitive material, or a plurality of photosensitizer or surface acting agents or the light dosage rate. Nitzan et al teach a method of photosensitizing cells using a photosensitizer-surfactant mixture which will perform as claimed (The PMNP, which is made from Polymyxin B sulfate will retain some of the polymyxin B therein, and thus is considered a mixture of a plurality of surfactants) except for the specific time period between the addition of two agents and the use of benzalkonium, it would have been obvious to the artisan of ordinary skill to employ benzalkonium chloride in the solution used in the method of Nitzan et al, since this will inhibit bacterial and fungal contamination of the solution and to make the interval between the addition of two agents between one and 30 minutes since this is not critical and

would allow the membranes to be permiabilized prior to addition of the dye or alternatively to employ the surfactants, dosage rate, and photosensitive agents of Nitzan et al in the method of Vogel et al, since Vogel et al specifically state the surfactants may be added, since this would improve gel properties and also to employ the photosensitize agents since this would yield a composition also useful against gram negative bacteria, as taught by Nitzan et al, thus producing a method such as claimed.

(10) Response to Argument

A) Standard for Review

Appellant argues that the examiner's position must be supported by "substantial evidence". The examiner respectfully submits that the applied rejections are supported by substantial evidence.

B) Claims 1-3, 5-7, 9, 11, 15, 16, 19, 20, 22-25, And 30-32 Are Properly Rejected Under 35 U.S.C. 102(b) As Being Anticipated By Vogel et al

It is argued by appellant that "[A]anticipation requires identity of the claimed process and a process of the prior art; the claimed process, including each step thereof must be embodied in a single reference.". Next appellant asserts that Vogel et al teaches an intravenous solution, which, when dispensed from multiple does containers, can contain antimicrobial agents in bacteriostatic or fungistatic concentrations. Further appellant notes that among the compounds used is benzalkonium chloride (0.01%). Firstly, the examiner respectfully notes that the administration route is parenteral, not intravenous. Secondly, the examiner respectfully notes that "all the disclosures of a reference must be evaluated for what they fairly teach one of ordinary skill in the art" (see In re Boe 148 USPQ 507, 510 CCPA

(1966)). The examiner further notes that Vogel et al undeniably teach topical formulations for the photosensitizer compounds taught therein (see for example column 13, lines 36-42). Lastly the examiner notes that the level of skill in the art is quite high, requiring not only 12 years of primary and secondary school, but 4 years of college, 4 more years of medical school, and additional years as an intern before qualifying as an oncologist treating patients with photodynamic therapy. Given these facts, it is clear that the admonition of Vogel et al to employ agents such as benzalkonium chloride in "multiple dose containers" would be equally applicable to topically applied compositions as to intravenous ones. Further, since topically applied compositions would not be hermetically sealed, as multiple dose intravenous preparations are, there would be additional motivation to include such antibacterial elements.

Further appellant argues that Vogel et al do not disclose the mechanism of passing photosensitive material into the cell interior. The examiner must respectfully note that since appellant has disclosed no particular environmental conditions which cause benzalkionium chloride to behave in this manner, it must be presumed to do so under normal conditions, else appellant's specification is fatally defective. Additionally, it is well understood that "the mere recitation of a newly discovered function or property, inherently possessed by things in the prior art, does not cause a claim drawn to distinguish over the prior art." (see In re Swinehart et al, (USPQ 226, 229 (CCPA 1971)). Thus any attempt by appellant to assert an inherent property, unrecited by the references applied, as the point of patentability must fail.

Appellant then continues, arguing that the parenteral embodiment of Vogel et al does not anticipate various claims, noting that these claims all recite a specific range of concentrations

of benzalkonium chloride.. However, no amount of argument can remove from the four corners of the reference that teaching that the compounds can be topically applied, nor that such compounds, when in containers holding multiple doses require antibacterial measures, such as benzalkonium chloride. It is also noted that appellant has construed the teachings of Vogel et al too narrowly: appellant has insisted on referring to the teachings of Vogel et al as disclosing "intravenous" administration. In fact the term "intravenous" does not occur in the Vogel et al disclosure. Vogel et al teach **parenteral** administration. As one of ordinary skill in the art is well aware, parenteral encompasses "By some other means than through the gastrointestinal tract; referring particularly to the introduction of substances into an organism by intravenous, subcutaneous, intramuscular, or intramedullary injection. [para (para-) + G. enteron,1 intestine]" (Stedman's Medical Dictionary, 26th Edition). And since the aim of photodynamic therapy is to administer photosensitizers and localize them in the neoplastic tissue (see Vogel et al column 1, lines 36-38), if a tumor were present in a subcutaneous area, or in a muscle, one of ordinary skill in the art would clearly administer the compound intramuscularly or subcutaneously, where the relative concentrations of the constituents would remain unaltered, as they would be isolated in the tissue and only be dispersed by diffusion. One of ordinary skill in the art would not administer the compound intravenously, since this would disperse it throughout the body, rather than localize it in the vicinity of the neoplastic tissue. Thus even assuming, *arguendo*, that one of ordinary skill in the art would not perceive a need for antibacterial measures in a multiple dose container of topically applied compound, one of ordinary skill in the art would still apply the intramuscular or subcutaneous injections to the tumors so situated.

With regard to the argument concerning the lack of explicit disclosure in Vogel et al of the activity of benzalkonium chloride, appellant argues that Vogel et al does not disclose this, asserting that "Vogel et al discloses IV [sic, parenteral] administration of a dye solution, containing trace amounts of benzalkonium chloride as an antimicrobial agent". However, since the teachings of Vogel et al are not limited to intravenous administration, as appellant would argue, this overly narrow interpretation of the teaching of Vogel et al is not persuasive. Clearly, the teachings of Vogel et al encompass scenarios wherein the compounds are injected directly to the site of the tumor, thereby providing the claimed concentration of surfactant, regardless of any additional teachings which would not result in such a concentration at the cell site, as argued by appellant.

C) The Claims Are Obvious Under 35 U.S.C. 103(a)

i) Claims 1-4, 5-7, 9, 11, 15, 16, 18-20, 22-25, 30-34, and 40-52 Are Obvious Under 35 U.S.C. 103(a) Over Wilk ('020) in combination with Wilk ('675) and Vogel et al

Appellant argues that there would be "no motivation to replace the IV solution of Vogel et al with the saline solution in [sic, sterilizing] Wilk ('675) or the sterilizing [sic, saline] solution of Wilk ('020)". However, the examiner has never proposed such a combination. As clearly set forth in the final rejection, the sterilizing procedure of Wilk ('020) is modified by the teachings of Wilk ('675) to include a sterilizing solution, as taught therein (see Wilk ('675), Abstract). Further, since Wilk ('675) teaches no particular sterilizing solution, that of Vogel, which will also enhance the light application sterilization would clearly be chosen by one of ordinary skill in the art. Thus, in contrast to arguments by appellant, suggesting that the saline solution of Wilk ('020) is the "sterilizing solution" discussed in the rejection, it is in fact the solution of Wilk

('675), which is specifically stated to be a sterilizing solution, which the examiner employs the specific solution of Vogel et al, as Wilk ('675) teaches no specific solution with which to sterilize the device.

Then appellant asserts that the examiner is engaging in hindsight reconstruction. The examiner must respectfully disagree. The two references to Wilk are clearly related sterilization procedures, while the reference to Vogel et al is directed to compounds which are recognized to act on viruses and bacteria (see Vogel et al column 3, lines 30-37 and column 36, lines 16-19, i.e. claims 11 and 12) and as such constitutes a "sterilizing solution". Continuing, appellant asserts "we have submitted a product listing sheet and a published article on benzalkonium chloride. Both publications state that benzalkonium chloride is an unacceptable sterilant of medical equipment." While appellant has not specified the submissions referred to, it appears that they are the two page NPL, submitted March 13, 2003 and the four page article to Acosta-Glo et al, submitted June 27, 2003. While the latter article does appear to teach against the use of benzalkonium chloride as a sterilant, the two page document states the contrary, specifying "[Used as a medical disinfectant]" under the **Stability** heading. But regardless of this, the proposed substitution is that of the solutions of Vogel et al, which are not only taught as, but claimed as effective treatments for warts (which are caused by viruses) and bacterial infections. Thus Vogel et al being an issued U. S. Patent, and enjoying the presumption of validity afforded all such documents, the contradictory evidence regarding disinfectant ability of only one component of the claimed compound, is insufficient to demonstrate the unsuitability for the claimed function of the mixture.

a) Claim 34 Is Obvious Under 35 U.S.C. 103(a) Over Wilk ('020) in combination with Wilk ('675) and Vogel et al

Arguing the claim 34 is separately patentable, appellant notes that the method of claim 34, which is a method for photodynamic disruption of cells, requires identifying an air filtration/decontamination device, as part of the step of identifying an area of cellular activity. However, it is noted that one of ordinary skill in the art is at least an oncologist (see the originally filed disclosure, page 1, third sentence under **FIELD OF THE INVENTION**, PGPub, page 1, third sentence in paragraph [0002]), who is a surgeon (originally filed disclosure, page 8, second full paragraph, PGPub, page 3, paragraph [0022], and originally filed disclosure, page 18, line 7, PGPub, page 7, paragraph [0062]), as such the training for one of ordinary skill in the art would require not only 12 years of primary and secondary school, but 4 years of college, 4 more years of medical school, and additional years as an intern before qualifying as an oncologist, oncological surgeon, or plastic surgeon, and as such one of ordinary skill in the art would also be keenly aware of the necessity of maintaining cancer patients and patients undergoing or recuperating from surgery free from bacteria or viruses that can cause infection, which would require the air to be free from these pathogens. Since it is well known that pathogens can travel by and breed in air handling systems, as was the case with Legionnaire's Disease, one of ordinary skill in the art would understand that these, too would need to be disinfected and maintained in a germ free state, and would thus apply known disinfecting procedures, such as that taught by the combination of Vogel et al, Wilk ('675), and Wilk ('020) to the air handling system.

b) Claims 42, 47, and 51 Are Obvious Under 35 U.S.C. 103(a) Over Wilk ('020) in combination with Wilk ('675) and Vogel et al

Then appellant argues that the "generally accepted definition" of the term "impregnation" is the process of saturating something with a substance. Thus, appellant reasons as none of the references teach surface impregnation of a prosthesis or catheter, these claims are patentable. The examiner must respectfully note that an obviousness determination must be made in the context of the knowledge of one of ordinary skill in the art at the time of the invention. Given that appellant has already placed such surface impregnation in the realm of knowledge of one of ordinary skill in the art at the time of the invention: "the use of lumen flush solutions including a combination of antimicrobial agents as well as anticoagulants is a known process. Another strategy has been to impregnate the surfaces of catheters with antimicrobial agents in order to prevent colonization and the formation of biofilm." (see the originally filed disclosure, page 4, the third and fourth sentences of the first full paragraph, and the PGPub, page 2, paragraph [0010], the third and fourth sentences), the use of the solution of the combination of Vogel et al, Wilk ('675), and Wilk ('020) would have been obvious. Similarly, the impregnation thereof on a prosthesis – the ultimate indwelling medical appliance, would be similarly obvious.

ii) Claims 1, 5, 10-15, 20, and 26-29 Are Obvious Under 35 U.S.C. 103(a) Over Vogel et al in combination with Nizan et al

With regard to this rejection appellant asserts that Vogel et al "does not teach or suggest the mechanism of introducing photosensitive material into a cell interior by application of benzalkonium chloride to compromise the cell membrane". While appellant claims these steps, the manipulation responsible for them is simply the bringing of the cell into contact with the

solution. Since Vogel et al teach a mixture as claimed, the introduction of the photosensitive material must proceed naturally from the contacting of the cell with the claimed solution, else there is an additional unclaimed and undisclosed step which is necessary to produce this result. If such is the case, then appellant's claims are incomplete and the claimed method is non-enabled by the specification as filed. With regard to the teachings of Nitzan et al, appellant asserts "Nitxan uses PMNP to bind the PMNP-DP complex to the outer cell wall, much as a membrane specific antibody would. Neither PNMP nor the PNMP-DP complex cause a disruption of the cytoplasmic cell membrane (pp94 1st column). Unlike the present invention, Nitzan teaches the use of a surfactant to assist the binding of the photosensitizer to the cell membrane exterior, i.e. the outer cell wall." (see the instant Brief, the paragraph bridging pages 22 and 23, emphasis in original). However, the examiner must respectfully submit that appellant has misconstrued the teachings of Nitzan et al and further that appellant is arguing limitations that are not present in the claims at bar. Firstly, with respect to Nitzan et al, it is clear that cellular membranes are taught as being disrupted by PMNP to allow DP to act on the interior membrane: "It is clear that PMNP disturbs and disorganizes (by its action) the outer-membrane structure of Gram-negative bacteria, as shown previously by others (Vaara and Vaara 1983a,b). In our case, without such disturbance of the outer membrane, DP cannot act on the inner membrane of these bacteria…Disruption of the outer membrane structure by PMNP allows the penetration of the porphyrin and consequently enables the killing of the Gram-negative bacteria." (see Nitzan et al, page 95, column 1, second full paragraph, emphasis added). Thus clearly not only does the surfactant PMNP disrupt the cell membrane, but Nitzan et al, as well as others prior to them were well aware of this effect. Further, the term "membrane", as used in the instant claims, cannot be

restricted to mean only the cytoplasmic membrane as argued by appellant: "The term 'membrane' as used herein is meant to broadly include cellular or acellular organism structures, such as cell walls, cytoplasmic membranes, cell envelopes, coverings, capsids, envelopes, or other types of boundary-defining terms of cellular or acellular organisms." (see the originally filed disclosure, page 15, the last full sentence, PGPub, page 6, the antepenultimate sentence in the paragraph bridging columns 1 and 2, internal quotes in original). Thus clearly, the "membrane" recited in the claims at bar cannot properly be read as narrowly as appellant is arguing.

Next appellant argues that there "must be some reason suggestion or motivation found in the prior art whereby a one of ordinary skill in the art would make the combination" (see the instant Brief, page 23, first full paragraph). However, it is well established that "Rigid application of "teaching, suggestion, or motivation" test, under which patent claim is proved obvious only if prior art, nature of problem addressed by inventor, or knowledge of person having ordinary skill in art reveals some motivation or suggestion to combine prior art teachings, is inconsistent with expansive and flexible "functional approach" to resolution of obviousness issue" (see KSR International Co. v Teleflex Inc. 82 USPQ2d 1385, 1385 (Supreme Court, 2007), internal quotes in original). Thus clearly one must not look merely to the "teaching, suggestion, or motivation" of the prior art, but the scope and content of the prior at, the differences between the claimed subject matter and the prior art and the level of skill of one of ordinary skill in the art. As already set forth above, the level of skill of one of ordinary skill in the art is quite high. It has also been established that (i) benzalkonium chloride is a surfactant (see the originally filed disclosure, page 8, first full paragraph, PGPub, page 3, paragraph [0023],

which gives an open ended list of exemplary surfactant compounds including benzalkonium chloride) and (ii) surfactants are known to permiabilize, disorient, and disrupt cell membranes, thereby allowing photosensitizers to pass therethrough ("Chemical agents, such as surfactants, are known to affect the permeability of cell membranes, and membrane-like structures of acellular organisms, such capsids and envelopes. The ability of these chemical agents or surfactants to become oriented between lipid and protein films is thought to produce a disorientation of the membrane of microorganisms, so that it no longer functions as an effective osmotic barrier."; see the originally filed disclosure, page 15, the penultimate full sentence, PGPub, page 6, the sentence just prior to the antepenultimate sentence in the paragraph bridging columns 1 and 2, emphasis added). Given these facts, coupled with the level of skill of one of ordinary skill in the art, the substitution of benzalkonium chloride for PMNP would merely be the substitution of one element (PMNP, which disorients cell membranes, as discussed by Nitzan et al, cited above) for another element recognized as having the same function (benzalkonium chloride, which is a surfactant that disorients cell membranes, as discussed in (ii) of this section, above), to yield predictable results. Thus while appellant may argue that the claims are not obvious over the cited references under the rigid TSM test, this is not the proper test for obviousness under 35 U.S.C. 103(a), as set forth in *KSR*. And under the functional approach, the claimed invention is obvious over the applied references.

Turning to the teachings of Vogel et al, appellant argues that Vogel et al do not teach the use of benzalkonium chloride to improve the viscosity of a gel. The examiner must respectfully disagree, as Vogel et al do teach the use of surfactants to improve gel properties, and since, as set forth in (i) of this section, above, benzalkonium chloride is a surfactant, while Vogel et al does

not contain the teaching ipsis verbis, the teaching is still fairly contained therein. With respect to the teachings of Nitzan et al, as above, appellant argues the claims far more narrowly than they are drafted, and as such the arguments are not convincing for this reason alone. However, they are further not convincing, because if the substitution of one well known membrane permiabilizing agent for another were made, the benzalkonium chloride must behave in the same way as in the claimed mixture, as appellant has disclosed no additional steps or conditions which provoke the chemical response described in the claims.

a) Claims 10 and 26 Are Obvious Under 35 U.S.C. 103(a) Over Vogel et al in combination with Nizan et al

The examiner has set forth a clear motivation for providing the claimed time interval between the addition of the two agents: "since this…would allow the membranes to be permiabilized prior to addition of the dye" and further noted that the claimed interval is not critical. In response appellant has merely asserted, without supporting showing, that the examiner has relied upon impermissible hindsight. Given that the examiner has articulated a clear and undisputed reason for the time interval, appellant's unsupported arguments are not convincing.

(11) Related Proceedings Appendix

NONE

(12) Conclusion

It is the examiner's firm opinion that the appealed claims are not patentable for the reasons argued above. Appellant has presented no convincing argument as to why the rejections set forth above are not obvious or proper. Therefore, it is respectfully submitted that the final rejection be affirmed.

Respectfully Submitted,

/david shay/

Primary Examiner, Art Unit 3769

David Shay
March 31, 20099

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